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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
08/796,040	02/05/1997	METIN COLPAN	P58126US1	8477

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EXAMINER	
CRANE, LAWRENCE E	
ART UNIT	PAPER NUMBER
1623	

DATE MAILED: 09/10/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	08/796,040	COLPAN, METIN	
	Examiner	Art Unit	
	L. E. Crane	1623	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *05/18/2004 (amdt)*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *120-138* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *120-138* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

No claims have been cancelled, claim **136** has been amended, the disclosure has not been amended, and no new claims have been added as per the amendment filed May 18, 2004. No additional Information Disclosure Statements (IDSs) have been received as of the mailing date of this Office action.

Claims **120-138** remain in the case.

The following is a quotation of 35 U.S.C. §103(**a**) which forms the basis for all obviousness rejections set forth in this Office action:

> "A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made."

Claims **120-138** are rejected under 35 U.S.C. §103(**a**) as being unpatentable over **Henco et al. '426** (PTO-892 ref. **I**) in view of **Little '430** (PTO-1449 ref. **AC**), and further in view of the International Dictionary of Medicine and Biology (PTO-892 ref. **S**) and **Hames et al.** (PTO-892 ref. **R**).

The instant claims are directed to a process for DNA purification with the following steps:
i) cell lysis using an enzyme (e.g. RNase A) or using a mixture of chemical reagents (e.g. buffered SDS) and debris removal using filtration and/or centrifugation;
ii) contacting the filtrate from step i) with an anion exchange resin in buffers of low ionic strength, and elution of the DNA from the anion exchange resin by contacting with a high-ionic-strength buffer, optionally following the addition of a lower alcohol, or of polyethylene glycol, and
iv) desalting the DNA-containing solution by contacting same with a mineral support material to effect adsorption of the DNA onto the mineral support material (e.g silica gel) followed by washing the adsorbed DNA with alcoholic solutions to remove salts, and elution of DNA from the mineral adsorbent by contacting the mineral support material with a low ionic strength buffer (e.g. buffered Tris) or with water.

Henco et al. '426 discloses a four step process summarized as follows:
i) cell lysis/filtration by any one of numerous known methods including the use of detergents, proteolytic enzymes or mechanical procedures (see claim 8) including centrifugation (see column 6, lines 51-66);
ii) anion exchange chromatography by transferring the product solution from step i) to an anion exchange resin followed by washing with a low ionic strength buffer the intended effect of which is to remove all of the interfering substances (e.g. RNA, proteins) from long chain DNA which remains adsorbed on the column optionally in the presence of known DNA precipitants polyethylene glycol or isopropanol (see col. 12, lines 41-42);
iii) elution of the long chain DNA from the anion exchange column adsorbent with high ionic strength buffer; and
iv) desalting the DNA by one of several different methods. One method of desalting not mentioned in the Henco disclosure is adsorption chromatography wherein a sample of DNA is applied to the column adsorbent such as silica gel in the presence of a high ionic strength buffer and separated therefrom by subsequent elution with low ionic strength buffer or water alone.

Little '430 at column 7, lines 12-45, discloses one of several examples wherein DNA is extracted from cells of various types using chaotropic ion/enzyme-mediated digestion followed by centrifugation and ultimately chromatographic separation using a commercial diatomaceous earth (Celite™) and various buffer solutions. As noted in the abstract, Little discloses the application of DNA to the adsorbent from a relative high ionic strength solution, washing to remove salts, and subsequent elution of the adsorbed DNA with a low ionic strength buffer or with water. This reference does not disclose the use of anion exchange resins to selectively retain DNA in a purification process.

To make clear the meaning of the **Henco et al. '426** disclosure two additional definitional references have been cited along with the relevant portion of Henco to provide a more complete basis for the instant rejection. The term "chaotropic" is defined in International Dictionary of Medicine and Biology, Vol. 1, at p. 522 to be a word describing an agent which " ... destroys the the order of water when dissolved in it and thereby raises the solubility of hydrophilic substances in the solution." Further definitional exemplification is provided by **Hames et al.** (Nucleic Acid Hybridisation - A Practical Approach) via the indexing of "Chaotropic agents" at p. 235, which refers to pages 64-65 wherein a list of compounds is

provided at p. 65, lines 10-12 and includes i) ethylene glycol, ii) sodium perchlorate, iii) tetramethylammonium chloride, iv) tetraethylammonium chloride and v) urea. (emphais added) The Henco reference does not make any generic reference to "chaotropic agents," but at column 8, line 61 Henco specifies "urea" as a component of the viral lysis mixture.

Applicant's combination of,
a) conventional cell lysis,
b) the physical separation of cell debris,
c) the anionic exchange chromatography of the filtrate isolated from the cell debris, and
d) finally desalting of the DNA-containing eluate form the anion exchange column by application to a chromatographic adsorbent (e.g. silica gel) to effect the desalting,
is a combination of process steps well known in the prior art and motivated generically by the disclosures of **Henco et al. '426**, with specific desalting step details disclosed by the **Little '430** reference. As noted supra, Henco does teach the use of DNA desalting subsequent to anion exchange. The failure to teach the specific desalting method of the instant claimed method by **Henco '426** has been addressed in the instant rejection of record by combining **Henco et al. '426** with the **Little '430** reference, wherein the latter reference discloses the utility of classical chromatography adsorbents for the purpose of isolating purified DNA in solutions with low net ionic strength. For this reason applicant's claimed process has been found to be nothing more than a combination of the **Henco '426** reference with **Little et al.'430**, wherein Henco provides the motivation to combine by noting the need to desalt the high-ionic-strength solution of DNA produced by anion exchange chromatography (see column 7, lines 44-46; or col. 12, lines 42-43). The specific details of washing steps, the timing of steps, the specific selection of wash solution contents, and the physical characteristics of the anion exchange resin and mineral adsorbent (e.g., particle diameter, pore size, etc.) are deemed to be variables clearly within the purview of the ordinary practitioner seeking to optimize the Henco and Little process steps for a specific situation. Therefore, the details of adsorbent choice, or other standard performance parameters (e.g. the frequency of washes, the variation of ionic strength in wash solutions, etc.) are deemed to be the kind of variables properly within the realm of routine experimentation by an ordinary practitioner in the course of optimizing the process steps disclosed in the prior art of record. For these reasons, the instant claims, in so far as they are directed to routine changes in experimental details of the kind noted above, are deemed to lack an adequate basis for a finding of patentable distinction

for any variation of the instant claimed process, as such variations are deemed to have been properly included within the scope of the noted prior art.

Therefore, the instant claimed process for DNA purification by anion exchange chromatography followed by desalting using an entirely conventional adsorption chromatographic process would have been obvious to one of ordinary skill in the art having the above cited references before him at the time the invention was made.

Applicant's arguments filed May 18, 2004 have been fully considered but they are not deemed to be persuasive.

Applicant analyzes the details of the cited prior art at great length and then concludes that the instant rejection constitutes impermissible hindsight reconstruction. In particular applicant asserts at page 13 of the instant response, last paragraph, that "[t]he rejection tries to take the word 'urea' completely out of context of the teaching of Henco to find an inherent feature," and then concludes that "[t]he rejection relies on a torturous combination of prior art teaching[s] using impermissible hindsight reconstruction to meet the limitatiosn of the present claims."

Examiner respectfully disagrees. The instant combination of only two primary references (Henco & Little) is presented in a very detailed fashion in order to particularly meet the detailed presentation of the instant claims. If applicant finds this to be torturous examiner regrets that this is applicant's view, but in response notes that there is a degree of simplification below which one cannot descend without thereby failing to meet the requirement of meeting every element of the claimed invention.

Applicant's amendment necessitated the new grounds of rejection. Accordingly, **THIS ACTION IS MADE FINAL**. Applicant is reminded of the extension of time policy as set forth in 37 C.F.R. §1.136(a).

A shortened statutory period for response to this final action is set to expire THREE MONTHS from the date of this action. In the event a first response is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to

37 C.F.R. §1.136(a) will be calculated from the mailing date of the advisory action. In no event will the statutory period for response expire later than SIX MONTHS from the date of this final action.

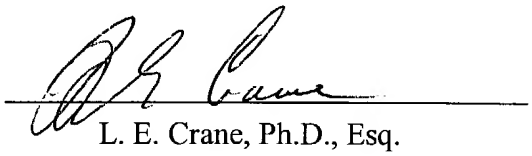
Papers related to this application may be submitted to Group 1600 via facsimile transmission (FAX). The transmission of such papers must conform with the notice published in the Official Gazette (1096 OG 30, November 15, 1989). The telephone number to FAX (unofficially) directly to Examiner's computer is 571-273-0651. The telephone number for sending an Official FAX to the PTO is 703-872-9306.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Examiner L. E. Crane whose telephone number is **571-272-0651**. The examiner can normally be reached between 9:30 AM and 5:00 PM, Monday through Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mr. James O. Wilson, can be reached at **571-272-0661**.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group 1600 receptionist whose telephone number is **571-272-1600**.

LECrane:lec
09/06/2004



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